REMARKS

In the most recently received (final) Official Action, the Examiners have rejected pending claims 11-12 respectively under a single basis - 35 U.S.C. 112, first paragraph - as being non-enabling for a defined family of short-length PR-39 derived oligopeptides.

In response, applicants have amended presently pending independent claims 11 and 12 respectively. By these claim amendments and the discussion presented hereinafter, applicants believe they have overcome and obviated the single basis for rejection stated by the Examiners in the most recent (final) Official Action.

I. A Preliminary Matter

Initially, and as a preliminary matter, applicants respectfully state that the Examiners of record have failed to acknowledge or to respond to applicants' formally presented and explicitly stated position concerning the basis and nature of the Examiners' self-imposed election of species.

Applicants, in their July 23, 2003 Response [to the Non-final Official Action mailed May 30th, 2003], have stated and maintained that: (i) The Examiners of record have unilaterally and without applicants' consent imposed an election of species; and, (ii) the Examiners have chosen to

misinterpret and wrongly presume that applicants' identification of SEQ ID NO:3 as one representative embodiment of the PR-39 derived oligopeptide family constitutes an election of species for that sequence alone for prosecution on the merits. Applicants again affirm that the Examiners' actions in this regard are erroneously based and completely unjustified.

Applicants also again respectfully submit and maintain that the Examiners actions and decisions are directly opposite to and contradict the Examiners' explicit statements and formal positions presented at page 4, 2nd paragraph of the Office Communication mailed April 7, 2003 - which demanded a Restriction Requirement, but did not ask for any election of species as such. Applicants' formal Response mailed April 15th, 2003 not only traversed the Restricted Requirement in its entirety, but also explicitly stated that Applicants did not then and do not now make any election of species whatsoever [Page 2, 2nd paragraph of the Reply mailed April 15, 2003].

The Examiners have clearly misread and misinterpreted applicants' written remarks and positions; and decidedly ignored and evaded from the Examiners' stated stance and explicitly expressed position. Moreover, it appears that the Examiners continue to believe that they can ignore and evade from their prior stated stance and legal position in the Office Communication mailed April 7th, 2003; and that the Examiners apparently

presume that they can arbitrarily alter and completely reverse their earlier-stated view and position whenever it suits them, at the Examiners' whim.

Despite this attempt as evasion, the Examiners' previously stated position is a matter of formal record; and remains factually and legally binding upon the Examiners as the "law of the case" under the legal doctrine of estoppel as well as by the legal constraints imposed by the prosecution file history to date. The Examiners' formally stated prior stance is not merely a minor item or trivial footnote which can be ignored and forgotten whenever it suits the Examiners' convenience.

Applicants' position is therefore directly opposite and contrary to the Examiners' present stance: The Examiners are factually constrained and are legally obligated to maintain a consistent position. Moreover, the Examiners have an overt duty and affirmative responsibility to meet and keep their word and commitments as stated.

For these reasons, applicants request that the Examiners of record reconsider their inconsistent position and formally reinstate dependent claims 13 and 14 respectively as presently pending claims in this application.

II. Applicants' Claimed Invention

Before the question of whether or not the Specification text provides sufficient enablement for pending claims 11 and 12 can be properly

answered, it is useful first to summarize briefly the essence of the instant invention in order to identify what applicants' invention actually is as well as to separate and distinguish the defined invention from what it is not.

Applicants' invention is claimed specifically as a "PR-39 derived oligopeptide family". This term, "PR-39 derived oligopeptide family", is defined by amended independent claim 11 as a combination of requisite elements and particular limitations; and comprises a family whose individual members cause a selective inhibition of protease-mediated degradation in-situ after introduction intracellularly to a viable cell. The full membership of the PR-39 derived oligopeptide family is presently defined by amended independent claim 1.

In comparison, one particular preferred embodiment and member of this family of short-length oligopeptides is defined by dependent claim 12; and is a precisely recited sequence of 15 amino acid residues. For reasons previously stated above, only the family definition recited by amended claim 11 and the preferred 15 residue length embodiment recited by amended claim 12 constitute the claims presently pending in this application.

In addition, it will be noted that the wording of presently amended independent claim 11 recites the commonly shared characteristics and properties for the short-length amino acid residue length structures comprising the membership of this family of peptides; and that claim 11

delineates a circumscribed membership which is size-limited, is functionally specific, and is structurally related as a family of pharmacologically active oligopeptides. The commonly shared characteristics and properties of the PR-39 derived oligopeptide family are overtly stated and individually set forth as requisite elements and specific limitations by amended independent claim 11and are recited as specific residues in sequence by amended dependent claim 12.

It will be appreciated also that amended independent claim 11 explicitly sets forth five specific requirements for each member constituting this family of derived oligopeptides. These requirements include: that the maximum length of each oligopeptide be less than 26 amino acid residues in length; that each oligopeptide begin with the sequence "Arg-Arg-Arg" at its N-terminal end; that each oligopeptide be devoid of the amino acid sequences "Pro-Pro-X-X-Pro-Pro-X-X-Pro" and " Pro-Pro-X-X-X-Pro-Pro-X-X-Pro" where X is any amino acid; that each oligopeptide be able to interact selectively in-situ with such proteasomes as are present within the cytoplasm of the cell; and that each oligopeptide be able to alter markedly the proteolytic degradation activity of these proteasomes such that a an increased expression of an identifiable peptide occurs in-situ as a consequence.

Amended dependent claim 12 is the 15 amino acid residue length

restatement of this broad definition; a recitation which complies fully and completely with the stated requirements of amended independent claim 11. Accordingly, amended claims 11 and 12 respectively present an accurate and precise recitation of applicants' inventive subject matter as a whole.

II. The Rejection Under 35 U.S.C. 112, 1st Paragraph, Enablement

The Examiners have rejected claims 11-12 under 35 U.S.C. 112, first paragraph, as allegedly failing to provide information sufficient to enable one skilled in the art to make and practice applicants' invention as claimed.

The Examiners have presented their views and position at pages 3-4 in the most recently received (final) Official Action. The essence of their stated rationale is a single sentence, without any additional explanation or further elaboration, which is reproduced below:

> "...Those skilled in the art are unlikely to accept the data as being correlatable to SEQ ID NO:3, a 15 amino acid residue and a family of PR-39 derived oligopeptides whose members cause a selective inhibition of proteasome-mediated degradation for at least one identifiable peptide in-situ after introduction intracellularly to a viable cell...." [page 3, lines 15-19 of the instant Official Action].

In response to the Examiners' stated rationale, applicants and their undersigned attorney respectfully submit the following:

First, the Examiners have employed legal standards which are subjective and do not conform to the correct and proper objective legal standards regarding adequacy of disclosure for enablement as prescribed by

statute and the governing caselaw decisions.

Second, the Examiners have failed to appreciate properly the totality of factual content disclosed by the Specification text, and have failed to give proper credence to the quality and quantity of the detailed information presented by the written disclosure.

Third, the Examiners have reviewed the pending claims and the Specification text from an erroneous perspective and from a vantage point which fails to recognize or take into account the ordinary skills and commonplace knowledge routinely available and conventionally employed in the relevant field by the practitioner.

Each of these major failures and errors will be demonstrated and explained in detail.

The legal errors of the Examiners:

Applicants respectfully submit that the Examiners have inadvertently and unfortunately departed from the proper legal standards and requirements of enablement; and presented applicants instead with a subjective view and improvised position which is flawed, erroneous and legally unsupportable. Applicants therefore offer the Examiners a true and correct statement of the objective legal standards by which sufficiency of enablement is to be determined.

1. Nothing more than objective enablement is required as a matter of law; and it is irrelevant whether this quantum of information is provided through a broadly written description and disclosure, or by illustrative examples, or by working experiments with observed empirical data [In re Wright, 27 U.S.P.Q. 2d 1510 (1993)]. Thus, there is no meaningful difference when determining the adequacy of description and information for enablement purposes whether a broadly written description in meaningful detail is provided by a Specification text; or if a series of illustrative hypothetical examples is presented in a variety of circumstances by the disclosure; or if a series of actual experiments with resulting empirical data and conclusions supported by the empirical data is given in any degree, quality or form by the written text. Any presentation of such information in any of these formats is legally and factually sufficient to satisfy the enablement requirement.

2. If and when the Examiners reject one or more claims because of the enablement requirement of Section 112, the Examiners bear the initial burden of setting forth a *prima facie* case and a reasonable explanation as to why they believe that the scope of protection defined by that claim is not adequately enabled by the description of the invention provided by the totality of information disclosed within the Specification text of the

application. The Examiners are thus legally required and obligated to present sufficient fact, reasoning and evidence about the objective truth of the information presented within the Specification text; to explain why the Examiners doubt the truth or accuracy of any statement in the disclosure of the Specification; and to back up such assertions with acceptable evidence or reasoning which is inconsistent with the information or statements disclosed by the Specification text.

It is thus incumbent on the Examiners to establish first a *prima facie* case of non-enablement. A mere statement, or opinion, or point of view by the Examiners that they personally believe that the disclosure is not enabling of itself, or is insufficient to support one or more specific claims, is not legally adequate or proper to meet the legal burden of presenting and supporting a *prima facie* case of non-enablement [In re Marzocchi, 169 U.S.P.Q. 369 (CCPA 1971); In re Sichert, 196 U.S.P. Q. 209 (CCPA 1977)].

3. It has been emphasized repeatedly by major caselaw decisions that the enablement requirement of Section 112, 1st paragraph does not require a specific example of everything possible within the scope of a broadly defined claim [In re Anderson, 176 U.S.P.Q. 331 (CCPA 1973)]; and that not even one single specific illustrative working example need be present within the disclosure of a specification text in order to meet and satisfy the enablement

requirement of Section 112 [In re Stephens, 188 U.S.P.Q. 659 (CCPA 1976)].

Moreover, the fact that a Specification text may be devoid of even one working or illustrative example is itself without legal significance. It is well established that illustrative examples, or empirical data, and the like are not legally necessary in order to have an enabling disclosure [In re Borkowski, 164 U.S.P.Q. 642 (CCPA 1970)]. Accordingly, the presence or absence of even a single illustrative embodiment or working example does not of itself provide any legal basis or support to explain why a Specification text is not enabling or to explain why the scope of the enablement is not commensurate with the scope of protection sought by the pending claims.

4. As a matter of long-established legal principle, there is no requirement under 35 U.S.C. 112, 1st paragraph that an inventor correctly set forth, or even know, how or why the claimed invention works or functions [Newman v. Quigg, 11 U.S.P.Q.2d 1340 (Fed. Cir. 1989)]. Moreover, it is axiomatic that an inventor need not even comprehend the scientific principles upon which the practical effectiveness of his invention rests [Fromson v. Advance Offset Plate, Inc., 219 U.S.P.Q.2d 1137 (Fed. Cir. 1983)]. Accordingly, therefore, no legal basis or duty of any kind exists for the written disclosure of a Specification to provide any explanation, or any

understanding, or even any theory of why the claimed invention works or how the claimed invention functions.

Furthermore, the presence of experimental details or other descriptive statements within a disclosure that a particular physiological phenomenon was observed and experimentally evaluated are not deemed to be "intrinsically suspect" simply because the underlying biomolecular basis for the empirical observation cannot be predicted or explained [In re Cortright, 49 U.S. P.Q.2d 1464 (Fed. Cir. 1999)]. Thus, the Examiners cannot overtly state or even suggest that the enablement requirement legally demands that applicants prove the mechanism of action involved or the nature of a function/structure relationship to account for the observed physiological activity and the consequential result caused by a defined composition of matter.

5. The enablement requirement of Section 112, 1st paragraph, also does not require that the disclosure of the Specification convince any person (including the Examiners) that the assertions, information, and knowledge contained therein are proven correct to the point of absolute certainty [In re Robins, 429 F.2d 452 (CCPA 1970)]. There is thus no legal requirement in law that the Examiners become completely persuaded; or become a committed follower; or be a true supporter of the scientific model, theory or

premise upon which an invention is based or of any mechanism of action upon which the invention relies.

Rather, the legal obligation and burden upon the Examiners is a quite different one entirely: the Examiners are required to evaluate the totality of the disclosure within the Specification text when evaluating whether the disclosure is adequate for purposes of enablement; and the purpose of the Examiners' evaluation is to determine objectively whether there is sufficient information, detail and knowledge disclosed within that text which would allow a person of ordinary skill in the pertinent art to make and use the invention as claimed.

6. It has long been recognized that the Examiners are neither permitted to act as nor intended to be either a scientific board of inquiry or an editorial review committee. Also, the purview of the Examiners' objective assessment is not intended or expected to delve into the details or minutiae which further experimentation or other additional empirical data might reveal or supply in terms of a greater appreciation of what the invention is and/or what might be the most optimal conditions of how the invention is to be practiced [In re Marzocchi, 169 U.S.P.Q. 367 (CCPA 1971); In re Brana, 34 U.S.P.Q.2d 1437 (Fed. Cir. 1995)].

Moreover, where the Examiners have expressed subjective doubt and

personal opinion regarding the nature of the invention, or the range of specific embodiments, or the number of illustrative examples embodying the invention - rather than objectively address and evaluate whether the totality of the Specification text provides adequate information as to how to make and use the invention as claimed – such a rejection is then without factual or legal support and is completely improper [In re Armbruster, 185, U.S.P.Q. 152 (CCPA 1975)].

7. Enablement is also legally satisfied and fulfilled when one possessed of the knowledge and information provided by the Specification text could use the invention as claimed without undue experimentation [In re Eynde, 178 U.S.P.Q. 470 (CCPA 1973)]. The objective determination of what constitutes "undue experimentation" in any given instance requires the application of the standard of reasonableness, having due regard for the nature of the invention as claimed and the state of the pertinent art.

This test is not merely quantitative since a considerable amount of experimentation is legally permissible. Thus, if such experimentation is merely routine or if the Specification text provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed, then such experimentation is not "undue". The key and essential word, therefore, is always "undue" and not "experimentation" [In re

Angstadt, 190 U.S.P.Q. 214 (CPPA 1976); Atlas Powder Company vs. E.I. DuPont DeNemours & Co., 224 U.S.P.Q. 409 (Fed. Cir. 1984); In re Wands, 8 U.S.P.Q. 2d 1400 (Fed. Cir. 1988)].

8. In addition, the mere possibility that a recited claim might include a large number of embodiments and use instances does not of itself prevent or legally deny the allowance of claims having a broad scope. Moreover, it is not incumbent on an applicant who has made a broad invention either to demonstrate with evidence or to prove with data (i) empirical support for the entire descriptive range of possibilities envisioned; or (ii) the degree of embodiment variation or the diversity of capabilities in every embodiment and use instance of the invention which may fall within the broad scope of the claims. The function of a recited claim is to point out what the invention is and to define the scope of the protection; it is not, however, intended to exclude conditions or instances which are possibly of no use in practicing the invention [In re Sarett, 327 F. 2d 1005 (CCPA 1964)].

Thus, when the degree of experimentation involved is commonplace, such as the personal selection of commonly available choices known in the field or which become available via a study of other routine parameters and variations that anyone ordinarily skilled in the pertinent art might expect, none of these experiments are "undue"; and the Specification disclosure, as

written, is legally adequate and factually sufficient to satisfy the enablement requirement [In re Geerdes, 180 U.S.P.Q. 789 (CCPA 1974); In re Morehouse, 545 F.2d 162 (CCPA 1976)].

The factual errors of the Examiners:

As applicants have shown and documented previously herein, the Specification text not only describes in detail the commonly shared characteristics and properties of the PR-39 derived oligopeptide family at page 25, lines 1-22; but also sets forth at page 26, lines 1-32 multiple illustrative examples and preferred embodiments of the membership which constitutes the PR-39 derived oligopeptide family as such. In addition, the commonly shared characteristics and properties of the PR-39 derived oligopeptide family described in detail at page 25, lines 12-22 of the Specification text are overtly restated and individually set forth; and this antecedent description corresponds and directly correlates with the requisite elements and specific limitations recited by amended independent claims 11 and 15 respectively.

Equally important, in opposition and contradiction to the Examiners' stated view, these specified traits and attributes for the membership as a whole constituting the PR-39 derived oligopeptide family also have been experimentally illustrated and empirically validated. Such evidence is

demonstrated by Experiment 6 and the use of PR-11, as described at page 46, lines 1-24 of the Specification. This particular working example and empirical demonstration of activity is not limited to merely this 11 residue peptide alone. To the contrary, this representative embodiment amply evidences and empirically demonstrates the requisite structure, function, and pharmacological activity for the entire PR-39 derived oligopeptide family membership as defined by amended independent claim 11 as well as for the preferred embodiment and 15 amino acid residue length recited by dependent claim 12.

It is important also for the Examiners to recognize and acknowledge that the other experiments and empirical results described by the Specification text at pages 40-46 constitute probative evidence of the traits and attributes of the membership constituting the PR-39 derived oligopeptide family as a whole; and such evidence clearly demonstrates the utility and functional capabilities for the entire membership of the PR-39 derived oligopeptide family defined broadly by amended independent claim 11 and in particular by dependent 12.

Applicants and their undersigned attorney therefore respectfully submit and affirm that an objective review and evaluation of the range of antecedent description and the variety of illustrative details disclosed by the Specification text reveals all the necessary knowledge and information

concerning the structure, attributes and traits of the oligopeptides defined by amended independent claim 11 and dependent claim 12 such that any ordinarily skilled practitioner could chose, prepare and use any member of the PR-39 derived oligopeptide family at will.

The prejudicial error in the Examiners' evaluation:

1. Applicants find that the Examiners' views and positions as stated within the instant Official Action (particularly at page 3, lines 15-22 and page 4, lines 1-6) merely represent the Examiners' subjective desire for recitations of unknown and non-essential technical details and information; and, moreover, constitute a request for a kind of incidental and supplemental information which can be routinely experimentally obtained on-demand and without major difficulty by any person ordinary skilled in this art – after he has read the broad and detailed description provided by the Specification text.

Applicants also submit and affirm that no legal justification or support exists in law for the Examiners' stated view that structure/activity data correlatable to SEQ ID NO:3 must be disclosed. To the contrary, applicants maintain that an enabling disclosure – as revealed by the controlling caselaw decisions - does not demand or legally require any description or inclusion of data showing a structure to activity relationship for any embodiment

disclosed within the Specification text in order to meet and satisfy the 1st paragraph of Section 112. The Examiners' stated position and stance is especially improper and unjustified concerning the 15 residue embodiment defined by claim 12 in view of the empirical results and demonstrated activity for the 11 amino acid residue peptide disclosed by the Specification text at page 46.

Moreover, by making such a demand and posing the demand as a legal requirement which must ostensibly be satisfied for enablement purposes, the Examiners have committed gross and prejudicial legal error. Applicants affirm that the Examiners are demonstrably without legal support, or proper cause, or lawful justification for their stated view and position.

2. It will be recognized and acknowledged that all the essential aspects of the invention defined by amended claims 11 and 12 respectively are disclosed in written descriptive detail; are structurally and functionally characterized in depth; and are revealed in multiple illustrative examples and embodiments by the Specification text. In addition, applicants have clearly shown that the Specification text provides specific parameters, guidance, and valuable insights for choosing, preparing and making any chosen embodiment of the PR-39 derived oligopeptide family – whenever the ordinarily skilled person in this technical field wishes to do so. Given this

totality of information, guidance and insight now existing within the Specification text, any ordinarily skilled in this art would have no need or use for a redundant experimental recitation directed to reaffirming a previously described and proven structure/activity relationship in order to make and use applicants' defined invention for its intended purpose.

Furthermore, applicants respectfully submit that the manner of making and using the present invention is revealed in full and explicated in depth by the range and variety of the experiments and empirical data disclosed by the Specification text. Thus, the practitioner ordinarily skilled in this art could easily prepare and utilize without major difficulty many different embodiments of the entire PR-39 derived oligopeptide family as a whole from the limited membership defined by amended independent claims 11 and 12 respectively.

3. Applicants also submit and maintain that the Specification text provides an abundance of detailed description and informative information as to how to make and use analogues of PR-39 which are shorter than 26 amino acid residues in length - which is the subject matter as a whole defined by the presently pending claims. Thus, so long as the each member of the PR-39 derived oligopeptide family is structurally a short-length analog of native PR-39, is pharmacologically active, and can interact with

proteasomes in the specified manner to achieve the desired result, there is no practical need for nor any informational value in multiple proofs of activity either within the disclosure or the membership defined by amended independent claims 11 and 12 respectively.

In summary, applicants respectfully submit and maintain that the Examiners have failed to adhere to or comply with the above-identified proper legal standards when conducting their assessment and evaluation of the claims pending in the present application. Instead, the Examiners have wrongly demanded more details; improperly insisted upon more working examples; and peremptorily required more information – all of which would constitute merely ordinary and routine experiments to yield merely a better appreciation of biomolecular mechanisms or activity/structure parameters; and provide, at most, an empirical showing of non-essential details for the relevant art. None of the Examiners' demands for such information, even if acquiesced to, would be of unusual or significant benefit to the practitioner in this field, given the quantity and quality of information and knowledge disclosed by the Specification text presently to the ordinarily skilled practitioner in the art.

For these reasons, applicants regretfully submit that the Examiners have made multiple factual and legal errors regarding the enablement

requirement for the invention as presently claimed. Accordingly, on the basis of all the foregoing, applicants request that the Examiners reconsider their position and withdraw this ground of rejection against the presently pending claims.

In sum, applicants have addressed the single basis of rejection stated in the most recently received (final) Official Action forthrightly and objectively. In applicants' view, this issue has been evaluated, acted upon and resolved completely. Accordingly, for these reasons, applicants respectfully submit and affirm that amended claims 11and 12 now pending are therefore now allowable.

In view of the above discussion and detailed review, applicants believe that this case is now in condition for allowance and reconsideration is respectfully requested. The Examiners are invited to call applicants' undersigned attorney should they feel that such a telephone call would further the prosecution of the present application.

Respectfully submitted,

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